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Inventors: Van Eyk et al.
Serial No.: 09/115,589
Filing Date: July 15, 1998
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This listing of the claims will replace all prior versions and listings of claims in the application:

Listing of the claims:

Claims 1-55 (canceled)

Claim 56: (previously presented) A method for assessing cardiac muscle damage in a subject, comprising detecting the presence or absence or measuring the amount of:

- (a) a peptide fragment of a myofilament protein; or
 - (b) a covalent or non-covalent complex of at least:
 - (i) a peptide fragment of a myofilament protein and an intact myofilament protein; or
 - (ii) two peptide fragments of myofilament proteins,
- in a biological sample obtained from a subject being assessed for cardiac muscle damage by incubating the biological sample with an antibody or a functional fragment of an antibody that specifically binds to the:
- (a) peptide fragment of a myofilament protein; or
 - (b) covalent or non-covalent complex of at least:
 - (i) a peptide fragment of a myofilament protein and an intact myofilament protein; or
 - (ii) two peptide fragments of myofilament proteins,

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under conditions which allow the antibody or functional fragment of the antibody to form a complex with the

(a) peptide fragment of a myofilament protein; or

(b) covalent or non-covalent complex of at least:

(i) a peptide fragment of a myofilament protein and an intact myofilament protein; or

(ii) two peptide fragments of myofilament proteins,

and detecting or measuring the formed complex,

wherein said peptide fragment of the myofilament protein or said peptide fragment of the covalent or non-covalent complex consists of:

all or a portion of a cardiac troponin I peptide fragment selected from the group consisting of SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26 and SEQ ID NO:27,

a myosin light chain 1 peptide fragment,

all or a portion of a troponin T peptide fragment selected from the group consisting of SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32 and SEQ ID NO:33,

a troponin C peptide fragment, or

an α -actinin peptide fragment,

and wherein the presence or amount of:

(a) the peptide fragment of the myofilament protein; or

(b) the covalent or non-covalent complex of at least:

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(i) the peptide fragment of the myofilament protein and the intact myofilament protein; or
(ii) two peptide fragments of myofilament proteins,
in the biological sample is associated with cardiac muscle damage.

Claim 57: (previously presented) The method of claim 56 wherein the presence of at least two different peptide fragments of myofilament proteins or covalent or non-covalent complexes is detected.

Claim 58: (previously presented) The method of claim 56 wherein the amounts of at least two different peptide fragments of myofilament proteins or covalent or non-covalent complexes are measured and the measured amounts are compared as an indication of the extent of cardiac muscle damage in the subject.

Claim 59: (previously presented) The method of claim 56 wherein the ratio of at least two different peptide fragments of myofilament proteins or covalent or non-covalent complexes is assessed as an indication of the extent of cardiac muscle damage in the subject.

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Claim 60-61: (canceled)

Claim 62: (previously presented) The method of claim 56, wherein the complex is detected or measured by assaying for the presence of a label.

Claim 63: (previously presented) The method of claim 56, wherein the compound is labeled with an enzyme which is detected by measuring enzymatic activity associated therewith.

Claim 64: (previously presented) The method of claim 63, wherein the enzyme is selected from the group consisting of alkaline phosphatase, horseradish peroxidase, luciferase, beta-galactosidase, lysozyme, glucose-6-phosphate dehydrogenase, lactate dehydrogenase, and urease.

Claim 65: (previously presented) The method of claim 56, wherein the antibody or functional fragment of an antibody is immobilized on a solid phase.

Claim 66: (previously presented) The method of claim 65, wherein the solid phase is a plastic surface.

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Claim 67: (previously presented) The method of claim 56, wherein the antibody or functional fragment of an antibody binds to a region of troponin I comprising all or a portion of SEQ ID NO:26 or SEQ ID NO:27.

Claim 68: (previously presented) The method of claim 56, wherein the antibody or functional fragment of an antibody the binds to a region of troponin I comprising all or a portion of SEQ ID NO:21.

Claim 69: (previously presented) The method of claim 56, wherein the antibody or functional fragment of an antibody binds to the peptide fragment of myosin light chain 1.

Claim 70: (canceled).

Claim 71: (previously presented) The method of claim 56 wherein the cardiac muscle damage is reversible.

Claim 72: (previously presented) The method of claim 71 wherein the cardiac muscle damage is due to at least one condition selected from the group consisting of hypoxia, hypoxemia, ischemia, fatigue and reperfusion.

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Claim 73: (previously presented) The method of claim 56 wherein the muscle damage is irreversible.

Claim 74: (previously presented) The method of claim 73 wherein the muscle damage is due to at least one condition selected from the group consisting of hypoxia, hypoxemia, ischemia, and reperfusion.

Claim 75: (previously presented) The method of claim 56 wherein the biological sample is selected from the group consisting of cardiac muscle tissue, a component of cardiac muscle tissue, blood, blood serum and urine.

Claim 76: (previously presented) The method of claim 56, wherein the peptide fragment of the myofilament protein or the covalent or non-covalent complex of at least:

(i) a peptide fragment of a myofilament protein and an intact myofilament protein; or

(ii) two peptide fragments of myofilament proteins consists of all or a portion of a cardiac troponin I peptide fragment selected from the group consisting of SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26 and SEQ ID NO:27.

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Claim 77: (previously presented) The method of claim 56, wherein the peptide fragment of the myofilament protein or the covalent or non-covalent complex of at least:

(i) a peptide fragment of a myofilament protein and an intact myofilament protein; or

(ii) two peptide fragments of myofilament proteins consists of a myosin light chain 1 peptide fragment.

Claim 78: (previously presented) The method of claim 56, wherein the peptide fragment of the myofilament protein or the covalent or non-covalent complex of at least:

(i) a peptide fragment of a myofilament protein and an intact myofilament protein; or

(ii) two peptide fragments of myofilament proteins consists of a covalent complex.

Claim 79: (previously presented) The method of claim 78 wherein the covalent complex consists of all or a portion of a cardiac troponin I peptide fragment selected from the group consisting of SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26 and SEQ ID NO:27 and a troponin C peptide fragment or a troponin T peptide fragment.

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Claim 80: (previously presented) A method for assessing skeletal muscle damage in a subject, comprising detecting the presence or absence or measuring the amount of:

- (a) a peptide fragment of a myofilament protein; or
- (b) a covalent or non-covalent complex of at least:
 - (i) a peptide fragment of a myofilament protein and an intact myofilament protein; or
 - (ii) two peptide fragments of myofilament proteins,

in a biological sample obtained from a subject being assessed for skeletal muscle damage by incubating the biological sample with an antibody or a functional fragment of an antibody that specifically binds to the:

- (a) peptide fragment of a myofilament protein; or
- (b) covalent or non-covalent complex of at least:
 - (i) a peptide fragment of a myofilament protein and an intact myofilament protein; or
 - (ii) two peptide fragments of myofilament proteins,

under conditions which allow the antibody or functional fragment of the antibody to form a complex with the

- (a) peptide fragment of a myofilament protein; or
- (b) covalent or non-covalent complex of at least:
 - (i) a peptide fragment of a myofilament protein and an intact myofilament protein; or

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(ii) two peptide fragments of myofilament proteins,
and detecting or measuring the formed complex,
wherein said peptide fragment of the myofilament protein or
said peptide fragment of the covalent or non-covalent
complex formation consists of:

- a troponin I peptide fragment,
- a myosin light chain 1 peptide fragment,
- a troponin T peptide fragment,
- a troponin C peptide fragment, or
- an α -actinin peptide fragment,

and wherein the presence or amount of:

- (a) the peptide fragment of the myofilament protein; or
- (b) the covalent or non-covalent complex of at least:

(i) the peptide fragment of the myofilament
protein and the intact myofilament protein; or

(ii) two peptide fragments of myofilament
proteins,

in the biological sample is associated with skeletal muscle
damage.

Claim 81: (previously presented) The method of claim
80, wherein the peptide fragment of the myofilament protein
or the covalent or non-covalent complex of at least:

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(i) a peptide fragment of a myofilament protein and an intact myofilament protein; or

(ii) two peptide fragments of myofilament proteins consists of a covalent complex.

Claim 82: (previously presented) The method of claim 80 wherein the presence of at least two different peptide fragments of myofilament proteins or covalent or non-covalent complexes is detected.

Claim 83: (previously presented) The method of claim 80 wherein the amounts of at least two different peptide fragments of myofilament proteins or covalent or non-covalent complexes are measured and the measured amounts are compared as an indication of the extent of skeletal muscle damage in the subject.

Claim 84: (previously presented) The method of claim 80 wherein the ratio of at least two different peptide fragments of myofilament proteins or covalent or non-covalent complexes is assessed as an indication of the extent of skeletal muscle damage in the subject.

Claim 85-86: (canceled)

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Claim 87: (previously presented) The method of claim 80, wherein the complex is detected or measured by assaying for the presence of a label.

Claim 88: (currently amended) The method of claim 80, wherein ~~the~~ the antibody or functional fragment of the antibody is labeled with an enzyme which is detected by measuring enzymatic activity associated therewith.

Claim 89: (previously presented) The method of claim 88, wherein the enzyme is selected from the group consisting of alkaline phosphatase, horseradish peroxidase, luciferase, beta-galactosidase, lysozyme, glucose-6-phosphate dehydrogenase, lactate dehydrogenase, and urease.

Claim 90: (previously presented) The method of claim 80, wherein the antibody or a functional fragment of an antibody is immobilized on a solid phase.

Claim 91: (previously presented) The method of claim 90, wherein the solid phase is a plastic surface.

Claim 92: (previously presented) The method of claim 80 wherein the skeletal muscle damage is reversible.

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Claim 93: (previously presented) The method of claim 92 wherein the skeletal muscle damage is due to at least one condition selected from the group consisting of hypoxia, hypoxemia, ischemia, fatigue and reperfusion.

Claim 94: (previously presented) The method of claim 80 wherein the skeletal muscle damage is irreversible.

Claim 95: (previously presented) The method of claim 94 wherein the skeletal muscle damage is due to at least one condition selected from the group consisting of hypoxia, hypoxemia, ischemia, and reperfusion.

Claim 96: (previously presented) The method of claim 80 wherein the biological sample is selected from the group consisting of skeletal muscle tissue, a component of skeletal muscle tissue, blood, blood serum and urine.

Claim 97: (previously presented) A method for assessing muscle damage in a subject, comprising detecting the presence or absence or measuring amounts of at least two different:

- (a) peptide fragments of a myofilament protein
- (b) covalent or non-covalent complexes of at least:

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(i) a peptide fragment of a myofilament protein and an intact myofilament protein; or

(ii) two peptide fragments of a myofilament protein,
in a biological sample obtained from a subject being assessed for muscle damage by incubating the biological sample with an antibody or a functional fragment of an antibody that specifically binds to the:

(a) peptide fragment of a myofilament protein; or

(b) covalent or non-covalent complex of at least:

(i) a peptide fragment of a myofilament protein and an intact myofilament protein; or

(ii) two peptide fragments of myofilament proteins,
under conditions which allow the antibody or functional fragment of the antibody to form a complex with the

(a) peptide fragment of a myofilament protein; or

(b) covalent or non-covalent complex of at least:

(i) a peptide fragment of a myofilament protein and an intact myofilament protein; or

(ii) two peptide fragments of myofilament proteins,

and detecting or measuring the formed complex,

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wherein said peptide fragments of the myofilament protein or said peptide fragments of the covalent or non-covalent complexes consist of:

troponin I peptide fragments,
myosin light chain 1 peptide fragments,
troponin T peptide fragments,
troponin C peptide fragments, or
 α -actinin peptide fragments,

wherein the presence or amount of the:

(a) peptide fragments of the myofilament protein; or
(b) covalent or non-covalent complexes of at least:
(i) the peptide fragment of the myofilament protein and the intact myofilament protein; or
(ii) two peptide fragments of the myofilament protein,
in the biological sample are associated with muscle damage,
and

wherein the

(a) peptide fragments of the myofilament protein; or
(b) covalent or non-covalent complexes of at least:
(i) the peptide fragment of the myofilament protein and the intact myofilament protein; or
(ii) two peptide fragments of the myofilament protein,
are from the same myofilament protein.

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Claim 98: (previously presented) The method of claim 97 wherein the ratio of the

(a) peptide fragments of the myofilament protein; or

(b) covalent or non-covalent complexes of at least:

(i) the peptide fragment of the myofilament protein and the intact myofilament protein; or

(ii) two peptide fragments of the myofilament protein,

from the same myofilament protein is assessed as an indication of the extent of the muscle damage in the subject.

Claim 99: (new) The method of claim 80 wherein the myofilament protein is a slow isoform of troponin I, troponin T or troponin C.

Claim 100: (new) The method of claim 80 wherein the myofilament protein is a fast isoform of troponin I, troponin T or troponin C.

Claim 101: (new) The method of claim 97 wherein the myofilament protein is a slow isoform of troponin I, troponin T or troponin C.

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Claim 102: (new) The method of claim 97 wherein the myofilament protein is a fast isoform of troponin I, troponin T or troponin C.